

NIH POLICY MANUAL

3044-1 - NONHUMAN PRIMATE QUARANTINE

Issuing Office: NCRR/VRP 496-9416

Release Date: 04/11/97

1. **Explanation of Material Transmitted:** This chapter describes NIH policies and procedures for quarantine of nonhuman primates (NHPs) for NIH operated Intramural Research Animal Programs (NIH IRP). This is a new issuance.
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A. Purpose:

This policy establishes the responsibilities and procedures for the quarantine of nonhuman primates (NHPs) for NIH operated Intramural Research Animal Program (NIH IRP). The National Center for Research Resources (NCRR) Veterinary Resources Program (VRP) and each NIH Institute, Center, and Division (ICD) that uses NHPs shall be responsible within its respective area for ensuring compliance with this policy.

B. Scope:

This policy applies to all NIH IRP operated animal programs. The NIH IRP animal programs operated outside the state of Maryland may quarantine and necropsy NHPs at their facilities, but they must adopt procedures consistent with this policy. Agencies

that lease space from NIH intramurally operated animal programs must comply with this policy or seek a variance from the Director of VRP as a term of the lease agreement.

C. Facilities:

Nonhuman primates quarantined by the VRP are quarantined at the NIH Animal Center (NIHAC) in Building 103. The NIH IRP animal programs operated outside of Maryland may quarantine NHPs at their facilities.

D. Procurement:

These procurement procedures apply to the NIHAC, Building 103. Similar procedures are followed at other locations.

To place an order or to otherwise have NHPs quarantined at the NIHAC, the ICD Animal Program Director (APD) or designee(s) shall submit a completed NIH Centralized Animal Order Request Form (Appendix 1) or equivalent to the Chief of the Primate Service Poolesville (Chief of the PSP). Prior to submission to the Chief of the PSP, the order shall be reviewed and approved by the ICD. A copy of an approved Animal Study Proposal (ASP) also shall be provided to the Chief of the PSP.

Prior to processing the order, the Chief of the PSP will review the request. The specifications of the animals to be procured must be completely and accurately described. The procurement of nonhuman primates also must comply with CDC requirements and USDA regulations (Appendix 2, References 3, 4). The Chief of the PSP will contact the ICD APD if the request is incomplete or not approved.

Macaque and African species, Apes, and New World Primates shall be obtained from breeding and conditioning programs in the country of origin and approved domestic sources (Appendix 3). VRP veterinarians will make site visits to suppliers as appropriate to evaluate their ability to meet NIH IRP requirements. Depending on the availability of animals, the time from placement of an order to completion of quarantine could be in excess of six months.

E. Entry Requirements:

Rhesus, Cynomolgus, and Pigtail macaques, provided under competitive contracts, shall have a history of negative tuberculin skin tests (TSTs). At least three (3) TSTs shall be performed, not less than two weeks apart, and one of the tests within 10 days prior to shipment. The supplier shall provide a complete copy of all procured animals' health records, including the origin and date of birth, if known.

Nonhuman primates provided under contract shall not have been subjected to experimental use. Macaque monkeys provided under contract shall be serologically negative and culture or PCR negative for SRV-1 and SRV-2, and seronegative for B virus (HSV), SIV and STLV-1. Evidence of freedom from other pathogens may be requested by the APDs and required by the Chief of the PSP.

All NHPs shall be checked immediately upon arrival at the NIHAC, Building 103, to ensure that they meet the order requirements. Animals judged healthy, after an examination by a Doctor of Veterinary Medicine at the time of arrival, including a review of their health records, a physical examination, and subsequent laboratory and TST tests, shall be accepted. Animals judged unacceptable shall be returned to the supplier, euthanized or treated in accordance with USDA regulations (Appendix 2, Reference 4) after the Chief of the PSP consults with the involved ICD APD and the supplier.

Animals should not be accepted from registered importers who are experiencing reportable diseases (Appendix 4) or significant losses of animals.

Nonhuman primates that leave an NIH ICD's animal facilities may reenter the ICD's animal facilities without repeating a standard quarantine period, if their history, inspection, and tests deemed necessary by the admitting veterinarian indicate that there has been no exposure to NHP or human pathogens. The ICD APD or designee(s) must seek approval for reentry from the Chief of the PSP.

Macaca, Ceropithecus, Erythrocebus, Papio, Saimiri, Cebus, Callithrix, Saquinus, and Ateles species born in NIH colonies will be vaccinated against rubeola virus (Attenuvax - Merck & Co., Inc., or equivalent) at six and nine months of age and tested at twelve months of age, unless the approved ASP requires rubeola naive animals. Animals that do not have a positive titer will be revaccinated.

F. Quarantine Requirements:

1. Quarantine and Stabilization:

All nonhuman primates that are introduced into NIH animal colonies located on the NIH campus in Bethesda or the NIHAC must be quarantined in Building 103 at the NIHAC, unless a variance is approved. The NIH IRP APD or designee(s) must contact the Chief of the PSP to arrange quarantine or request a variance.

Groups of nonhuman primates in quarantine shall be maintained separately from other NHPs. Cohorts should be separated by source, geographic origin, date of arrival, and presumptive health status. Quarantine and stabilization shall be conducted in a manner that complies with the NRC Guide (Appendix 2, Reference 10). It shall provide sufficient time for acclimation, evaluation of animal health, and expression of diseases.

Animals shall be individually housed during quarantine.

Ninety days is the standard length of quarantine for newly acquired vervets, macaques and chimpanzees. Sixty days is the standard for baboons, patas monkeys, prosimians, and New World Primates. The history of the quarantined animals and the source may be considered when any variation in the length of quarantine is being determined.

Extension of quarantine may be appropriate for NHPs with incomplete histories and cohorts that develop disease during quarantine. Quarantine shall be reinstated, or the affected NHPs euthanized, when diseases that pose a threat to the NIH NHP colony or

to humans are detected.

Procedures shall include a TST using a minimum of 0.1 ml of USDA licensed and approved Old Tuberculin (OT) administered 14 days apart in alternate eyelids, and continued until a minimum of five consecutive negative results have been recorded. For quarantined chimpanzees, the last two TSTs shall be administered a month apart.

Test sites shall be examined 24, 48, and 72 hours after administration of OT. The TST results may be recorded using the California scoring system (Appendix 2, Reference 2); however, a written description of the TST results must be provided with the score. Refer to the guidelines for the "Prevention and Control of Tuberculosis in Nonhuman Primates in the NIH Intramural Program". Appendix 2, Reference 13) for interpretation of TST results. Weights shall be recorded with the TSTs.

Quarantined NHPs shall have CBC, chemistry, and virus profiles (Appendix 5) submitted to VRP's Diagnostic Services, or an approved reference laboratory, within the first 30 days of quarantine; the samples will be taken to assure that those animals remain serologically and culture or PCR negative for those viruses listed in Appendix 5. The attending veterinarian may perform other diagnostic procedures when indicated. Those animals harboring pathogens shall be rejected or treated after consultation with the involved ICD APD or designee and the supplier.

After an initial acclimation period of 14 days, investigators may request that procedures such as feeding of special diets and blood collections be performed. Nonhuman primates also can have their behavior evaluated during routine quarantine. These procedures must be approved by the Chief of the PSP, and be performed by VRP personnel.

After a quarantined group of NHPs have completed 5 tuberculin tests administered at two week intervals with negative results, all *Macaca*, *Ceropithecus*, *Erythrocebus*, *Papio*, *Saimiri*, *Cebus*, *Callithrix*, *Saquinus*, and *Ateles* species shall be vaccinated against rubeola virus (Attenuvax - Merck & Co., Inc., or equivalent) unless the approved ASP requires rubeola naive animals. In the case of the latter, such animals shall be quarantined separately with appropriate quarantine measures to guard against exposure to rubeola.

2. Separation by Geographic Origin and Source:

Different NHP groups (different geographic origin, source, or arrival dates) shall be quarantined separately, whenever possible. If different NHP groups are maintained in the same room, the quarantine period shall begin on the date the last group was placed in the room. Involved investigators and APDs shall be notified before cohorts are combined. Cohorts may be combined only to avoid delays in delivery.

3. Necropsy:

All nonhuman primates that die or are euthanized in quarantine must be necropsied.

4. Tuberculosis Treatment and Isolation:

Nonhuman primates shall not be treated for tuberculosis without an ASP approved by the user ICD's Animal Care and Use Committee (ACUC) and the Institutional Biosafety Committee (IBC). Handling, transportation, housing and treatment of tuberculous NHPs must be conducted in accordance with instructions of the IBC. Animals with positive TSTs that are not treated should be immediately euthanized after consultation between the ICD APD and the Chief of the PSP, unless placed on an approved ASP.

5. Husbandry:

Only designated facility personnel shall be permitted in quarantine rooms. They shall comply with NIH Manual Chapter 3044-2, Protection of NIH Personnel Who Work with Nonhuman Primates (Appendix 2, Reference 9), and applicable guidelines for the prevention and control of tuberculosis in nonhuman primates in the NIH intramural program.

6. Enrichment:

NHPs shall be provided toys, novel food treats, and visual contact during quarantine in compliance with USDA regulations (Appendix 2, Reference 3). They shall not be group housed during quarantine.

G. Variance to Standard Quarantine:

1. Variance:

The Chief of the PSP and an ICD APD may agree to shorten or modify quarantine, when the circumstances support it. The principal investigator, through the ICD APD, must request a variance. If the Chief of the PSP denies the request, or if the Chief of the PSP and the ICD APD cannot agree on the terms of the NIH policy variance, then the ICD APD may refer the matter to the Chief of Laboratory Animal Services, Poolesville, for a decision. If no agreement is reached after these efforts, the issue shall be sent to the Director of VRP for a final decision.

2. Waivers:

Quarantine shall not be waived.

H. Facility Access:

Access to the VRP quarantine facilities shall be limited to authorized personnel, as determined by the Chief of the PSP.

I. Records Retention and Disposal:

For this chapter, records pertaining to "Veterinary Services" are retained and disposed of under the authority of NIH Manual 1743, "Keeping and Destroying Records," Item 3000-C. See manual for specific instructions.

Appendix 1:

See paper copy.

Appendix 2 - References:

- 1 1995 Buyer's Guide. Lab Animal 23(11):18,22.
2. Corcoran, KD, Jaax, GP. 1991. An attempt to predict anergy in tuberculosis suspect cynomolgus monkeys. Lab Anim Sci 41(1):57-62.
3. Title 9, Code of Federal Regulations, Subchapter A, Animal Welfare.
4. Center for Disease Control and Prevention (CDC). Oct., 1991. Update: Nonhuman primate importation: modified special permit requirements for importation and quarantine of nonhuman primates. MMWR.
5. CDC/NIH. 1993. Biosafety in Microbiological and Biomedical Laboratories.
6. Institute for Laboratory Animal Resources. 1980. Laboratory Animal Management: Nonhuman Primates. ILAR NEWS 23(2-3):P22-P24;P27-P29.
7. Martin, DP. 1986, 2nd ed. Quarantine and Tuberculosis. In: Fowler, ME (ed). Zoo & Wild Animal Medicine. Philadelphia: W.B. Saunders Company, 667-673.
8. Moreland, AF. 1970. Tuberculosis in New World primates. Lab Anim Care 19:629-634.
9. NIH Manual Chapter 3044-2, Protection of NIH Personnel Who Work with Nonhuman Primates.
10. The Guide for the Care and Use of Laboratory Animals. NRC 1996, 58-60.
11. Wolf, RH, et al. 1988. Multidrug chemotherapy of tuberculosis in rhesus monkeys. Lab Anim Sci 38(1):25-33.
12. March 1994 NIH "Report of the Animal Program Directors' Subcommittee on Nonhuman Primate Tuberculosis."
13. "Guidelines for the Prevention and Control of Tuberculosis in Nonhuman Primates in the NIH Intramural Program" NIH ARAC Guidelines 1996.

Appendix 3 - Species Availability and Sources:

Contact the Chief, PSP, about current availability of species, sources, and specifications. The following list is not intended to be limiting.

Baboons

Buckshire Corp. - DE*

Charles River Primates Corp. - ABCDE

Southwest Foundations of Biomedical Research - BCD

Chimpanzees

Buckshire Corp. - CE
Coulston Foundation - ABCE

Cynomolgus macaques

Buckshire Corp. - BCDE
Charles River Primates Corp. - ABCDE
Primate Products, Inc. - ABCDE
HRP, Inc. (current contractor) - ABCDE

Pig-tailed macaques

Buckshire Corp. - DE
Charles River primates Corp. - ABCDE
Primate Products, Inc - ABCDE
HRP, Inc. (current contractor) - ABCDE

Rhesus macaques

Buckshire Corp - BCE
Charles River Primates Corp. - BCDE
Primate Products, Inc. - ABCDE
HRP, Inc. (current contractor) - ABCDE

*A = specific pathogen free
B = health status reports
C = colony-bred, domestic
D = colony-bred in country of origin, imported
E = tuberculin skin tested

Marmosets

Buckshire Corp. - CE*
Charles River Primates Corp. - BCDE

Squirrel monkeys

Buckshire Corp. - CE
Charles River Primates Corp. - BDE

African green monkeys (vervets)

Buckshire Corp. - DE
Charles River Primates Corp. - BCDE

Patas monkeys

Charles River Primates Corp. - BDE

*A = specific pathogen free

B = health status reports

C = colony-bred, domestic

D = colony-bred in country of origin, imported

E = tuberculin skin tested

Appendix 4 - Reportable Diseases:

Registered importers must maintain records on each shipment of imported nonhuman primates received. Registered importers must notify The Center for Disease Control and Prevention (CDC), Division of Quarantine by phone (404-639-1437) or voice mail (404-330-2705) within 24 hours of the occurrence of any illness in nonhuman primates that is suspected of being yellow fever, monkeypox, or hemorrhagic fever (Marburg/Ebola). In addition, if mortality for a shipment exceeds five percent, the importer must immediately report the circumstances, including cause(s) of death to CDC. These requirements are established by Federal regulation (Title 42, Code of Federal Regulations, Section 71.53).

Appendix 5 - Simian Virus Screening Profiles (*1):

The following is the current list of viral serology tests recommended to screen NIH IRP NHP colonies; the list is subject to change by the APD's Committee:

*Asian Macaques(*1):*

Rhesus - SIV(mac), SRV1/SRV2(*2), B-virus, (HSV), Rubeola, STLV-1

Cynomolgus - Same

Pigtails - Same

Mauritius Macaques:

Cynomolgus - SIV(mac), SRV1/SRV2(*2), B-virus, (HSV), Rubeola, STLV-1

African Species:

Chimpanzees - HIV, Hepatitis A, HSV-1, HSV-2, Rubeola, VZV, EBV, RSV, SA8, Parainfluenza 1&3

Baboons - SHF, SA8, SIV, Rubeola

Patas - SHF, SIV, Rubeola

Sooty Mangabeys - SIV(sm), Rubeola

African Green Monkeys - SHF, SIV(agm), Rubeola

Galagos - Foamyvirus, Rubella

New World Primates:

Squirrel monkeys - H. Tamarinus, H. saimiri, Rubeola
Owl monkeys - Same
Marmosets - Same

(*1) Consider filovirus-like testing for rhesus and cynomolgus macaques, and African green monkeys. Include HIV for chimpanzees with incomplete histories. Chimpanzees also are susceptible to Hepatitis B, C (non-A, non-B), Delta, and E as well as A. Note that SRV5 is pathogenic to rhesus macaques of Indian origin, and is carried by cynomolgus macaques and rhesus monkeys of Chinese origin.

(*2) Isolation with initial serological profile recommended. Western blots may be requested, when serological results are indeterminate. Virus isolation can be completed in two to three weeks, and serology in three days.

Appendix 6 - Definitions:

Macaques: Nonhuman primates of the genus *Macaca*. Currently, they are imported only from China, Indonesia, the Philippines, and Mauritius. Domestic breeders may provide rhesus monkeys of Indian lineage.

African Species: Includes apes (chimpanzees) and prosimians (galagos).

Viruses:

SIV	Simian Immunodeficiency Virus
SRV	Simian Retrovirus
CMV	Cytomegalovirus
HSV	Herpesvirus simiae
HSV-1	Herpesvirus simplex 1
HSV-2	Herpesvirus simplex 2
STLV-1	Simian T-Cell Leukemia Virus
SA8	African Monkey Herpesvirus
EBV	Epstein-Barr Virus
VZV	Simian Varicella-Zoster Virus
RSV	Respiratory Syncytial Virus
HIV	Human Immunodeficiency Virus
Measles	Rubeola

Last Updated: 12/13/99

NIH